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Dibromochloropropane (DBCP)
Position Document 1

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This Position Document addresses the risks and benefits of pesticide products containing the subject active ingredient. The Agency has determined that the use of products containing the subject active ingredient may meet or exceed a risk criterion described in 40 CFR Part 154. Potential hazards will be examined further to determine the nature and extent of the risk, and considering the benefits of the subject active ingredient, whether such risks cause unreasonable adverse effects on the environment.				
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DIBROMOCHLOROPROPANE (DBCP)

POSITION DOCUMENT 1

Office of Pesticides and Toxic Substances
Environmental Protection Agency
Washington, D.C. 20460
September 22, 1977

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Dibromochloropropane (DBCP): Position Document 1

I. BACKGROUND

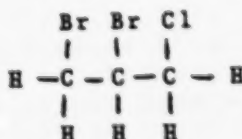
A. Characteristics

(1) Nomenclature

Dibromochloropropane (DBCP) is the trivial name for 1,2-dibromo-3-chloropropane. It is a soil fumigant. Some of its trade and experimental names are Fumazone (Dow), Nemagon (Shell), Nemaflow, Nemaset, Nematox, BBC 12 and OS-1897. The NIOSH number is TX87500 and the Chemical Abstracts number is 96128.

(2) Chemistry

DBCP, a liquid, is made by the liquid phase addition of bromine to allyl chloride. It is amber to dark brown with a slightly pungent odor. The molecular formula is $C_3H_4Br_2Cl$ and its molecular weight is 236.36. Its structural formula is



DBCP boils at 196 °C. Its vapor pressure is 0.8 mm at 21 °C.

and its flash point is 82 °C. DBCP is slightly soluble in water (0.1% w/w), but is miscible with aliphatic and aromatic hydrocarbons, oils, 1,2-di-chloropropane, isopropyl alcohol, tetrachloroethylene and 1,1,2-trichloroethane. Formulations include emulsifiable concentrates, liquid concentrates, solids, cakes and granules.

(3) Tolerances and Food Residues

Residues of inorganic bromides in or on raw agricultural commodities grown in soil treated with DBCP are established in 40 CFR 180.197 as:

5 ppm - apricots, nectarines and peaches.
10 ppm - walnuts and strawberries
25 ppm - blackberries, boysenberries, cotton, cucum-
bers, dewberries, grapes, loganberries, raspberries and
squash (summer).
50 ppm - tomatoes, cabbage, pineapples, cauliflower, -
peppers, eggplant, peanuts, melons, broccoli and brussel
sprouts.
75 ppm - almond hulls, beans (snap and lima), car-
rots, celery, figs, radishes, okra, parsnips, banana pulp
and turnips.
125 ppm - bananas (of which residue not more than
75 ppm shall be in the pulp after the peel is removed
and discarded), and soybeans.
130 ppm - endive (escarole) and lettuce.

There are no tolerances for inorganic bromides in meat
and milk to cover residues from use of peanut hay or peanut
hulls as cattle feed. Thus, DBCP and ethylene dibromide may
not be represented, sold or used for that purpose (40 CFR
180.126a).

As described in Section II below, the Shell and Dow
Chemical Companies jointly petitioned FDA to establish most
of these tolerances in 1961. The petitioners obtained
approval for their request after demonstrating (1) that no
residues of organic bromine (i.e., the parent compound DBCP)
were detected in any of the crops being petitioned and (2)
that total residues of the bromide ion (i.e., inorganic
bromine) on the petitioned crops were present at safe
levels. At that time, the analytical method for detecting
parent DBCP was sensitive from 0.2 to 1.0 ppm, depending
upon the crop being measured (Dow Chemical Co. 1961).
Total inorganic bromide residues were determined by modifi-
cations of the methods of Shrader et al. (1942) and of Mapes
and Shrader (1957).

Since that time, however, Hodges and Lear (1973) have
reported a method of detecting parent DBCP at level of
sensitivity of 0.001 ppm and at a validated level of 0.01
ppm. Using these methods, Newsome et al. (1977) have mea-
sured parent DBCP in radish and carrot crops after applica-
tion to muck soil at a rate of 12.26 lb/acre. Residues were
highest in carrots (1.5 ppm); after DBCP application at
seeding, they persisted for 16 weeks. DBCP disappeared from
the carrots more rapidly than from the soil. Foliage of both
crops contained smaller amounts than the root. 78% of the
DBCP in carrot was in the root. About two-thirds of the
residue was removed by boiling.

There are no tolerances for inorganic bromides in meat and milk to cover residues from use of peanut hay or peanut hulls as cattle feed. Thus, DBCP and ethylene dibromide may not be represented, sold or used for that purpose (40 CFR 180.126a).

The recommended maximum permissible daily intake of inorganic bromide in total human diet is 75 ppm (1.1 mg/kg) (Memo Sept. 13, 1961). The average human intake of bromide ion has been determined as 24 mg/day (Duggan and Lipscomb 1969).

(4) Degradation, Transport and Residues

DBCP injected into the soil DBCP persists for approximately 40 weeks (Hodges and Lear 1973, 1974). When applied by flood irrigation or by sprinkler, DBCP does not deeply penetrate the soil; rather, it is retained either near the soil surface or is lost to the atmosphere.

DBCP was converted by soil-water cultures to n-propanol, bromide and chloride. Maximum conversion was 63% after 4 weeks. Allyl alcohol was seen in some experiments as an intermediate, and was converted to n-propanol (Castro and Belser 1968).

(5) Metabolism

The distribution and metabolism of DBCP in rats is being traced in a study conducted for the National Cancer Institute (Lipscomb et al. 1977). Most of the animal tissues accumulate DBCP from one to three hours after an intraperitoneal dose. The intestine, liver and kidneys contain relatively large amounts. Most *in vivo* binding takes place in the RNA, DNA and protein of kidneys and liver. The liver microsomes catalyze a reaction which produces a product that has not yet been identified.

(6) Toxicity

All tests, including those discussed in Section III or IV, are summarized in Table 1.

The sensitivity of agricultural crops, ornamentals and turf to DBCP varies widely. DBCP is phytotoxic to certain plant species and should not be used on tobacco, onion, garlic, sugar beets, table beets, sweet potatoes, white potatoes, dwarf palm (Neanthella), Chamaedora elegans, chrysanthemum or Collinia elegans.

A concentration of 3 mg/l DBCP in water has no significant effect on biochemical oxygen demand, saprophytic microflora or nitrification processes (Rakhmatullayev 1969).

Smell and taste thresholds are 0.01 mg/l in water (Rakhmatullayev 1969). Dow Chemical Company has reported that DBCP is detectable by humans in air between 0.01 and 0.03 parts per million (Pers. Comm. 1977).

Cases of human exposure are discussed in Section III.

B. Registered Uses and Production

(1) Products

There are 72 Federal and 95 State registered products containing DBCP. 63 companies hold these registrations. There are 6 products registered for special local needs under section 24(c) of FIFRA.

(2) Use Patterns

The major uses of DBCP are as a soil fumigant nematocide on soybeans, pineapples, peaches, grapes, and citrus. Minor uses of DBCP include turf, ornamentals and vegetable crops.

(3) Supply

Dow Chemical and Shell Chemical companies are the sole manufacturers of DBCP in the United States. They have voluntarily ceased production and sales and have recalled all stocks from their distributors. The only known foreign supplier is located in Israel.

Table 1. Toxicological Test Results for DBCP

Test	Dose Levels and Duration	Species	Sex and number	Results	Source
Acute oral LD-50	DNS*	Rat	M	170-300 mg/kg	Torkelson 1961
	DNS	Rat	M/F	350 mg/kg	Rakhatullayev 1969
	DNS	Rat	F	260-410 mg/kg	Torkelson 1961
	DNS	Rat	M/F	380 mg/kg	Rakhatullayev 1969
	DNS	Rabbit	M/F	180 mg/kg	Torkelson 1961
	DNS	Guinea Pig	M	210 mg/kg.	Torkelson 1961
	DNS	Guinea Pig	M/F	316 mg/kg	Rakhatullayev 1969
	DNS	Chicken	unsorted	60 mg/kg	Torkelson 1961
	DNS	Mallard duckling	M/F	66.8 mg/kg	Tucker and Crabtree 1970
Skin Irri- tation	0.5 ml undiluted DBCP, 20 applications	Rabbit	4 animals	No erythema on intact skin; slight erythema on abraded skin; micro- scopic effects more severe.	Torkelson 1961
Eye Irri- tation	1.0% DBCP in propylene glycol	Rabbit	not given	Slight irritation of the conjunctiva and iris.	Torkelson 1961
Acute dermal	Undiluted DBCP, for 24 hr	Rabbit	not given	LD-50 = 1400 mg/kg	Torkelson 1961

* DNS = doses not specified

Table 1. (Continued)

Test	Dose Levels and Duration	Species	Sex and number	Results	Source
Subacute dermal	0.25 g DBCP, 10 24 hr applications	Rabbit	not given	Slight hyperemia and scaliness	Torkelson 1961
Acute inhal- ation	DNS	Rats	M	Eye and respiratory irritation seen at 60 ppm; kidneys permanently scarred at 50 ppm. LC-50 = 103 ppm LC-50 = 154 ppm LC-50 = 232 ppm LC-50 = 368 ppm	Torkelson 1961
Repeated inhalation	8 hr exposure 4 hr exposure 2 hr exposure 1 hr exposure 0, 5, 10, 20 and 40 ppm; 50 exposures over 7 wk	Rats	15 M per dose group	Gross lesions in lungs, intestinal mucosa, kidneys and testes at 10, 20 and 40 ppm. Testes atrophied at 20 and 40 ppm. testicular weight reduced in some males at 5 ppm.	Torkelson 1961
	0 and 12 ppm; 66 exposures over 70-92 days	Rats	20 M, 20 F	Lung weights significantly greater than controls at 12 ppm; marked pathological changes occurred in testes	Torkelson 1961
	0 and 12 ppm; 66 exposures over 70-92 days	Rabbits	3M, 3F	Severe atrophy and degeneration of testes at 12 ppm	Torkelson 1961

Table 1. (Continued)

Test	Dose Levels and Duration	Species	Sex and number	Results	Source
	12 ppm; 66 exposures over 70-92 days	G. Pig	10M + 10F	Severe atrophy and degeneration of testes at 12 ppm.	Torkelson 1961
	12 ppm; 50 and 60 exposures over 70-92 days	Monkey	2F	Developed severe secondary infections; aplastic anemia evident	Torkelson 1961
Intramuscular injec.	25 mg/kg for 3 days, repeated	Rat	5M + 5F	No significant hematologic changes	Torkelson 1961
Sub-chronic Ingestion	0, 5, 20, 50, 150 450 and 1350 ppm in diet for 90 days	Rat	14M + 14F per dose	Weight gain retarded at 150 ppm for F, and at 1450 ppm for M and F. Minimal cloudy swelling in 5 male livers and in several F kidneys.	Torkelson 1961
	70, 35 and 17.5 mg/kg perorally for 10 weeks	Rat	10M/dose	High dose produced necrotic changes in the parenchymatous organs and testes; other doses disturbed blood cell counts, liver function and nucleic acids.	Rakhmatullayev 1970
	0, 0.005, 0.05, 0.5 and 5.0 ppm for 8 months	Rat	7M/dose	Adverse effects on testes at 5 mg/kg, diminished fertility at 0.5 mg/kg and no testicular effect at .05 mg/kg. Kidneys, liver, reflexes and blood disturbed at dose as low as 0.05 mg/kg.	Rakhmatullayev 1970

Table 1. (Continued)

Test	Dose Levels and Duration	Species	Sex and number	Results	Source
Acute aquatic	100 ppm; 72 hr.	Redeared sunfish	20 fish per dose	No toxic effect	McCann, 1970
	32-180 ppm; 24 hr	Rainbow trout	-	LC-50 = 115.00 ppm	McCann, 1977
	48 hr			LC-50 = 85.00 ppm	
	96 hr			LC-50 = 36.50 ppm	
	0.25, 0.50, 1, 2.5, 5 and 10 ppm;	Clam	-	Larvae survival was 14% at 1 ppm and 1% at 2.5 ppm	Davis and Hidu 1969
	DNS; 24 hr	Bass	20 fish per dose	TLm = 30-50 ppm	Davis and Hardcastle 1959
	48 hr		TLm = 20 ppm		
	DNS; 24 hr	Bluegill	20 fish per dose	TLm = 50-125 ppm	Davis and Hardcastle 1959 Nishiuchi and Yoshida 1972
	48 hr		TLm = 20 ppm		
	DNS; 48 hr at 22 C.	I. exustus	-	TLm = 57 ppm	
S. libertina			TLm = 50 ppm		
C. malleata			TLm = 53 ppm		
P. acuta			TLm = 24 ppm		
	(all freshwater snails)				Alexander 1973
10, 20, 30, 40, 60, 80 and 100 ppm; 72 hr	Lake emerald shiners	5 fish per dose	Toxic effects at 20 ppm; LC-100 = 60 ppm.		
0, 6.5, 7.5, 10.0, 12.0 and 14.0 ppm for 24, 48 and 96 hr	Pink Shrimp	5 shrimp per dose	96 hr LC-50 = 12.7 ppm	Heitmuller 1974	

Table 1. (Continued)

Test	Dose Levels and Duration	Species	Sex and number	Results	Source
Acute aquatic	100 ppm; 72 hr.	Reared sunfish	20 fish per dose	No toxic effect	McCann, 1970
	32-180 ppm; 24 hr	Rainbow trout	-	LC-50 = 115.00 ppm LC-50 = 85.00 ppm LC-50 = 36.50 ppm	McCann, 1977
	0.25, 0.50, 1, 2.5, 5 and 10 ppm;	Clam	-	Larvae survival was 14% at 1 ppm and 5% at 2.5 ppm	Davis and Hidu 1969
	DNS; 24 hr 48 hr	Bass	20 fish per dose	TLm = 30-50 ppm TLm = 20 ppm	Davis and Hardcastle 1959
	DNS; 24 hr 48 hr	Bluegill	20 fish per dose	TLm = 50-125 ppm TLm = 20 ppm TLm = 57 ppm TLm = 50 ppm TLm = 53 ppm TLm = 24 ppm	Davis and Hardcastle 1959 Nishiuchi and Yoshida 1972
	DNS; 48 hr at 22 C.	I. exustus S. libertina C. malleata P. acuta (all freshwater snails)	-		Alexander 1973
	10, 20, 30, 40, 60, 80 and 100 ppm; 72 hr	Lake emerald shiners	5 fish per dose	Toxic effects at 20 ppm; LC-100 = 60 ppm.	Heitmuller 1974
	0, 6.5, 7.5, 10.0, 12.0 and 14.0 ppm for 24, 48 and 96 hr	Pink Shrimp	5 shrimp per dose	96 hr LC-50 = 12.7 ppm	

II. REGULATORY HISTORY

February 6, 1961 - Shell and Dow jointly petitioned FDA for the establishment of tolerances for residues occurring from application of DBCP in 44 crops. Toxicology data included studies by Torkelson et al. (1961) showing the hazards of DBCP: single application to eyes, single and repeated application to skin, single and repeated oral administration, single and repeated inhalation of vapors, and measurement of sensory threshold values. No comments were made by FDA reviewers.

March 1, 1961 - FDA prefilig review memorandum stated that the tolerances will be for inorganic bromides resulting from application of DBCP. Data submitted by petitioners showed that DBCP is not sorbed or translocated into crops regardless of application technique. The analytical methods used for detecting the inorganic bromides and parent DBCP are described in Section I.A.3.

March 16, 1961 - Federal Register Notice of Filing. Petition number assigned.

April 28, 1961 - USDA certified usefulness of DBCP and gave the opinion that proposed tolerances reasonably reflect the amounts of residues of total bromides.

August 30, 1961 - FDA memorandum reviewed method of analysis and residue data for inorganic bromides.

September 18, 1961 - FDA Toxicology Branch memorandum concluded that proposed inorganic bromide tolerances are safe for humans.

August 30, 1961 - FDA memorandum reviewed method of analysis and residue data for inorganic bromides.

September 18, 1961 - FDA Toxicology Branch memorandum concluded that proposed inorganic bromide tolerances are safe for humans.

April 11, 1963 - FDA Toxicology Branch memorandum concluded that use of Nemagon may increase content of inorganic bromides in cows' milk but that the bromide level will still be low enough that the milk is safe even for infants on an all-milk diet.

April 15, 1963 - Briefing memorandum to Commissioner of Food and Drugs recommended establishment of inorganic bromide residues.

May 18, 1963 - Proposed tolerances announced in Federal Register.

August 19, 1963 - University of California requested increase in tolerance for citrus. In a memo of conference dated September 6, 1973, Dr. O. G. Fitzhugh discussed a meeting with Dow concerning raising the citrus tolerance and concluded that no reproduction test would be required based on the long and extensive use of bromides and the presumed absence of parent DBCP residues.

September 16, 1964 - Application for registration of Shell's Nemagon.

September 26, 1964 - Registration issued for Shell's Nemagon.

March 28, 1967 - Federal Register Notice established tolerance of 50 ppm for inorganic bromide residues on broccoli, brussel sprouts, cabbage, cauliflower, eggplants, melons, peanuts, peppers, pineapples, tomatoes.

June 2, 1965 - Federal Register Notice increased tolerance on citrus from 5 ppm to 20 ppm.

August 24, 1966 - Approval granted for use on citrus fruits (limited to western states)

December 19, 1966 - Request granted for citrus and strawberries.

Feb. 9, 1967 - Approval of 50 ppm tolerance for all melons.

April 10, 1970 - Approval of tolerances for almonds, plums and prunes.

February 7, 1973 - Tolerances established and accepted for soybeans and lima beans.

May 25, 1973 - Dow submitted registration application for Fumazone F, a DBCP product intended for manufacturing use

only. Included with the submission was a reprint of the 1961 Torkelson study. A registration was issued for the product on August 29, 1973. The jacket file contains no record of any comment regarding the toxicology study. No chronic feeding or oncogenicity studies were submitted by any registrants.

April 15, 1976 - DBCP was identified by EPA as a candidate for RPAR based on potential for carcinogenic effects. No cancer studies had been submitted by anyone at that time, but published preliminary data from NCI was available in the literature.

November, 1976 - OSPR letter to registrants requesting adverse data.

January, 1977 - Shell submitted data in response to request.

July 26, 1977 - Dow responded with letter and progress report on animal studies to request.

August 1, 1977 - Occidental Chemical Company transmitted to EPA a telex notice of substantial risk of injury to human health from DBCP. This notice was pursuant to the requirements of the Federal Insecticide, Fungicide and Rodenticide Act and the Toxic Substances Control Act.

August 11, 1977 - Dow halted production and sales.

August 12, 1977 - California Department of Food and Agriculture announced a suspension of all sale and use of DBCP, urging that the public and dealers return all stocks to distributors.

August 16, 1977 - EPA, OSHA and NIOSH met to form a task force. Since then these agencies have been interchanging information on all levels.

August 24, 1977 - EPA received a petition from the Public Citizen's Health Research Group to suspend the registration of DBCP based on "human evidence of sterility and animal evidence of carcinogenicity..." (Letter 1977).

August 25, 1977 - Dow announced a recall of all DBCP from its users and distributors. OSPR sent letters to Dow, Shell and Occidental requesting all new data within 7 working days.

August 26, 1977 - Shell announced a recall of all DBCP.

III. SUMMARY OF EVIDENCE TO SUPPORT REBUTTABLE PRESUMPTION

A. Chronic Effects

(1) Oncogenicity

49 CFR 162.22 (a)(3)(ii)(A) provides that a "rebuttable presumption shall arise if a pesticide's ingredient(s) . . . (i)nduces onocogenic effects in experimental mammalian species or in man as a result of oral, inhalation, or dermal exposure" Section 162.3(bb) defines the term oncogenic as "the property of a substance or a mixture of substances to produce or induce benign or malignant tumor formation in living animals."

The following studies have been examined by the Working Group and collectively present evidence which meets the above criterion.

(a) NCI Bioassay on Rats and Mice

An NCI study was conducted at Hazleton Laboratories on Osborne-Mendel rats and (C57BL X C3H)F-1 mice between 1972 and 1974. Two dose levels, 30 and 15 mg/kg/day for rats and 260 and 130 mg/kg/day for mice, were selected. 50 males and 50 females of each species were placed in these treatment groups and in the control (untreated) groups. The animals received DBCP via stomach tube 5 days per week. When gross tumors were observed in an animal, it was immediately sacrificed. Dosing was stopped after 78 weeks for the rats and mice. The rats were observed for another 32 weeks and then sacrificed, while the mice were observed 12 weeks before sacrifice.

Several participants in this study have reported the results obtained at different stages of the bioassay. Olsen et al. (1973) first reported stomach cancer in both the rats and mice after only 10 weeks. They also observed a high incidence of mammary adenocarcinomas in female rats. Ward and Habermann (1974), the pathologists for the same study, reported that DBCP was "very carcinogenic." Powers et al. (1975) stated that after termination of the study, stomach squamous cell carcinomas were in excess of 60% in

rats and 90% in mice treated with DBCP; they also cited a high incidence (54%) of mammary gland adenocarcinomas in female rats. Weisburger (1977), in a draft report presented at a National Cancer Institute Seminar, reported in more detail the same findings.

The Carcinogen Assessment Group of EPA has summarized the results: "DBCP causes a significant increase in the incidence of gastric carcinomas in both sexes of rats and mice. Metastases of these tumors are reported. The tumor rates appear to be very high. A significant increase in the mammary cancer rate was also found in female rats" (CAG 1977).

(b) Hazleton Labs Bioassay on Rats and Mice

A second bioassay on rats and mice, funded by Dow Chemical Co., is currently in progress at Hazleton Labs. Four groups of 60 male and 60 female albino rats were dosed with 0, 0.3, 1.0 or 3.0 mg/kg/day DBCP in the diet. The study was terminated at 104 weeks in June 1977. A 78-week progress report received by OSPR July 21, 1977 describes the incidences of "possible neoplasms" in the liver, kidneys and stomach, based on a review by Hazleton of the gross necropsy sheets (Letter 1977). Significantly higher incidences of stomach tumors were reported for males and females receiving 1.0 and 3.0 mg/kg/day, but not in those receiving 0.3 mg/kg/day (CAG 1977).

The study on mice began on June 28, 1976 and is scheduled to be terminated in December, 1977. 50 males and 50 females were fed DBCP in the diet at 0, 0.3, 1.0 and 3.0 mg/kg/day. No signs of tumor induction were observed as of the 52nd week according to a progress report received by OSPR August 17, 1977 (Letter 1977).

(c) NCI Inhalation Carcinogenic Bioassay

An inhalation test using DBCP is now several months in progress. Protocols for the experiment are not available.

(2) Reproductive Effects

40 CFR 162.11(a)(3)(ii)(B) provides that "a rebuttable presumption shall arise if a pesticide's ingredients... [p]roduces any other chronic or delayed toxic effect in

test animals at any dosage up to a level as determined by the Administrator which is substantially higher than that to which humans can reasonably be anticipated to be exposed taking into account ample margins of safety."

The Working Group finds that, because sufficient data do not exist for determining a "no-effect" level of the reproductive effects of DBCP via either inhalation, dermal or oral exposure, acceptable levels of exposure may not be calculated for persons applying DBCP. Further, the Working Group asserts that there are effects at dosages up to a level substantially higher than that to which humans can reasonably be anticipated to be exposed taking into account "ample margins of safety." Therefore a rebuttable presumption exists for all products containing this compound. The following discussion demonstrates current levels of risk from exposure, the results of animal tests and the preliminary results of medical investigations at pesticide formulating plants.

(a) Risk Analysis

A preliminary risk analysis on DBCP by the Criteria and Evaluation Division on the potential human exposure to the use of DBCP concludes that pesticide applicators could be exposed to measurable quantities for short-term periods (Table 2). However, this exposure is 1,000 to 10,000 times lower than the levels to which factory workers are exposed. The dietary exposure of the general population is very much lower than that of applicators or field workers.

(b) Human Exposures

Three major producers of DBCP have been conducting medical examinations of their employees to detect any adverse effects from exposure to this and/or other chemicals during their manufacture or use. While official reports have not been received by the Agency, preliminary communications from these companies indicate the following findings:

1. Occidental Chemical Co.-- At the formulating plant in Lathrop, California, Dr. Wharton has examined 41 employees, of which 3 were females and 11 were males with vasectomies. 23 male individuals were actively working in the production area. 13 of these have exhibited oligospermia or aspermia. The potential causative agents have been narrowed down to DBCP, ethylene dibromide and carbaryl (Memo 1977).

Table 2. Samples of Approximate Human Exposures to DBCP
in Comparison to Rat Laboratory Data

Group	Size	Route	Dose/Duration	Total dose (mg/kg/yr)	Assumptions
Rat	---	inhal- ation	7.66 mg/kg/day for 90 days	460	Breathing rate of 0.073 l/min; avg. wt. of 0.2 kg per rat
Factory workers	?	inhal- ation	1.96 mg/kg/day for 240 days	470	Estimated air level of 0.9 ppm DBCP in factory; minute volume of man (light work) = 28.6 l/min; average weight = 70 kg; all inhaled DBCP retained
Soybean appli- cators	10,000	inhal- ation	0.18 mg/hr for 12.5 hrs. (appli- cation) + 18.0 mg/hr for 1 hour (mix and load)	.29	Same as above
Pineapple applicators	40	inhal- ation	18 mg/hr for 2 hrs. (mix and load)	0.5	Same as above
Soil irrigation applicators	4,000	inhal- ation	4.3 mg/day for one day	.06	Same as above; except air level estimated at 0.03 ppm
U.S. popu- lation	220,000,000	ingest- ion	0.0000022-0.0000061 mg/kg/day for 365 days	.0008- .002	Based on actual residue data for all foods treated with DBCP

2. Dow -- 12 of 14 workers at Dow's Magnolia, Arkansas examined preliminarily to date show reduced counts (Memo 1977).

3. Shell -- The first sperm counts from employees exposed to DBCP indicate 16 of 21 males tested have counts lower than would normally be expected (Shell 1977).

EPA has identified 22 incidents between April 1966 and August 1, 1976 in which DBCP was involved. 14 episodes occurred on agricultural areas, 3 in transit, 2 in storage areas, 1 at a land company site, 1 in the home and 1 at an unspecified site. Of these episodes, 20 involved DBCP alone and 2 DBCP in combination with other active ingredients. Acute effects observed include chemical burns, eye, nose, and throat irritation, nausea, chills, swelling, abdominal cramps, diarrhea, and death. A cause-effect relationship has not been confirmed between the pesticide and reported reactions for all of those incidents.

(c) Animal Studies

Torkelson et al. (1961) conducted several tests for Dow and Shell Chemical Companies. With reference to the inhalation exposure studies the authors noted that "the most striking observation at autopsy was severe atrophy and degeneration of the testes of all species."

Briefly, the different tests and their results were:

1. Groups of 15 rats exposed to DBCP vapors of 0, 5, 10, 20 or 40 ppm for a total of 50 exposures over 70 days showed gross lesions in lungs, intestinal mucosa, kidneys and testes at the 10 ppm dosage and higher dosages. Testes atrophied at 20 and 40 ppm, while testicular weight was reduced in some males at 5 ppm.

2. 20 male rats exposed to 12 ppm DBCP vapors 50 times over 70 to 92 days showed significantly greater lung weights than the treated groups. In males, the testicular weight was not significantly different from the controls, but marked pathological changes (not specified) were noted in the testes.

3. 3 male rabbits exposed to 12 ppm DBCP vapors 66 times over 70 to 92 days showed severe atrophy and degeneration of the testes.

4. 10 male guinea pigs exposed to 12 ppm over 70 to 92 days DBCP vapors 66 times showed severe testicular atrophy and degeneration.

A Russian study reports a subacute experiment of 45 days (Faydysh et al. 1970). 20 male rats were divided into a control and a treated group. The 10 treated rats received 70 mg/kg DBCP daily (1/5 the LD-50) in an oil solution. 5 animals died within 20-25 days after the start of the experiment. From a morphological study of the organs of treated rats, pathological degradation was observed in the testes and parenchymatous organs (kidneys). Further, a regeneration process arose in the organs of animals who survived the DBCP dosing.

A second Russian author has reported the results of single and chronic (8 months) oral exposures of DBCP to rats (Rakhmatullayev 1971). The chronic test used levels of 5.0, 0.5, 0.05 and 0.005 mg/kg. Severe effects were noted at the two upper levels. No effects were seen at the 0.005 level. White blood cell counts, conditioned reflexes and "generative function" were affected at 0.05 mg/kg, but gonadal measurements (testicular weight, spermatility, length of testes and testicular morphology) were not.

A third Russian team has reported significant injury to male and female sex gland activity in rats given 100 mg/kg DBCP once perorally and to another group given multiple doses of 10 mg/kg over 4 to 5 months (Reznik and Sprinchan 1975).

For males acutely exposed to 100 mg/kg, the concentration of spermatozoa in the ejaculate dropped sharply. After one week it was 2,617,000/ml in treated rats versus 4,870,000/ml in the control animals ($p < .001$); after two weeks the concentrations did not change and were 2,847,000/ml and 4,850,000/ml, respectively. Also, the duration of spermatozoon mobility decreased sharply, varying from about 10 to 20 minutes for treated rats and from 30 to 33 minutes for controls ($p < .01$). Thus, the final phases of spermatogenesis were damaged and the spermatozoon function destroyed by the acute exposure..

94.5% of females exposed once to 100 mg/kg developed atypical estrous cycles. The average number of complete cycles per female dropped and the stages of estrus and diestrus were extended. The stage sequence was destroyed for many of the females.

The function of the testes were also damaged from the chronic exposures. After 2 months the concentration of spermatozoa gradually decreased to 4,500,000/ml in the treated males versus 5,400,000/ml in the controls ($p < .01$); after 4 months it decreased to 2,480,000/ml in the treated animals, compared to 4,890,000 in the controls ($p < .001$). The mobility of the sperm of treated rats was significantly less than those of the controls ($p < .01$ and $p < .001$ at 2 and 4 months, respectively). In addition to alterations in the functional state of the spermatozoa, changes were observed in the process of spermatogenesis, such as decreases in the index of spermatogenesis and the average number of spermatogonia, as well as the appearance of degenerated cells in the spermatic epithelium. Biochemical changes were also noted, including an increase in the amount of acidic and alkaline phosphatase in the testicles and ejaculate in the third and fourth months.

The report was not clear as to whether the effects on the female reproductive system from chronic exposure to DBCP differed from the effects of the acute exposure.

IV. EVIDENCE INSUFFICIENT TO SUPPORT REBUTTABLE PRESUMPTION

A. Acute Effects

(1) Humans and Domestic Animals

DBCP does not meet the inhalation or dermal toxicity criteria (Torkelson et al. 1961).

(2) Wildlife

DBCP does not meet or exceed any risk criteria for wildlife.

B. Chronic Effects

(1) Mutagenicity

DBCP induces mutations in pol A - in strain TA1530 of

E. coli (Rosenkranz 1975) and in strain TA1530, TA 1538
of Salmonella typhimurium (Prival et al. 1977) and TA100 of

Salmonella (Blum and Ames 1977). However, these bacterial tests do not constitute adequate multitest evidence to support a rebuttable presumption. A sex-linked recessive lethal test and a heritable translocation test are recommended.

. (2) Wildlife Effects

Existing information does not suggest significant reductions in non-target organisms could be anticipated. These data are summarized in Table 1.

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